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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,100	01/31/2005	John W. Adams	AREN-027 (027.US2.PCT)	4553

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EXAMINER	
LI, RUIXIANG	
ART UNIT	**PAPER NUMBER**
1646	

MAIL DATE	DELIVERY MODE
03/05/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/523,100	ADAMS ET AL.	
	Examiner	Art Unit	
	RUIXIANG LI	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *132-152* is/are pending in the application.

4a) Of the above claim(s) *148-152* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *132-147* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06/08/2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/08/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

Applicants' amendment filed on 06/08/2007 has been entered in full. Claims 85-131 are canceled. Claims 132-152 are added. Claims 132-147 are currently under consideration. Claims 148-152 are withdrawn from consideration because they are drawn to non-elected invention.

Withdrawn Objections and/or Rejections

All the rejections set forth in the previous office action mailed on 12/21/2006 are made moot by cancellation of the claims.

Information Disclosure Statement

The information disclosure statement filed on 06/08/2007 has been considered by the examiner.

Drawings

The drawings filed on 06/08/2007 are accepted by the examiner.

Election/Restrictions

Applicants continue to traverse the restriction requirement. Since the restriction is made final in the previous office action, it is no longer arguable.

Claim Rejections Under 35 U.S.C.§112, 1st Paragraph (Written Description)

(i). The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(ii). Claims 132-139 and 145-147 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. Possession may be shown, for example, by describing an actual reduction to practice of the claimed invention. A specification may describe an actual reduction to practice by showing that the inventor constructed an embodiment or performed a process that met all the limitations of the claim and determined that the invention would work for its intended purpose.

It is not the case here. Claims 132-139 and 145-147 are drawn to a method comprising (a) contacting a candidate compound with a G protein-coupled receptor comprising an

amino acid sequence having at least 90% identity to SEQ ID NO: 3, wherein said GPCR is present on a cell or isolated membrane thereof; (b) determining the ability of the compound to modulate the G protein-coupled receptor; and (c) determining if said compound has cardioprotective activity. Since there is no nexus between (b) and (c), the claims, as written, encompass two different unrelated methods: determining the ability of a compound to modulate the G protein-coupled receptor and determining if a compound has cardioprotective activity. The instant disclosure fails to describe an actual reduction to practice of the claimed invention. There is no showing that the inventor constructed an embodiment or performed a process that met all the limitations of the claim and determined that the invention would work for its intended purpose. Accordingly, one skilled in the art would not recognize from the disclosure that the Applicants were in possession of the claimed methods at the time the application was filed.

(iii). Claims 132-134 and 136-147 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial

structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

Claims 132-134 and 136-147 are drawn to a method comprising determining the ability of the compound to modulate a G protein-coupled receptor comprising an amino acid sequence with at least 90% identity to SEQ ID NO: 3. Thus, the claims are drawn to a method of using a genus of variants or homologues of GPCR of SEQ ID NO: 3. The claims do not require that GPCR variants or homologues possess any particular biological activity, nor any particular conserved structure, nor other disclosed distinguishing feature.

The instant disclosure of two human RUP41 GPCR polypeptides set forth in SEQ ID NO: 2 and 3 and a mouse RUP41 GPCR polypeptide set forth in SEQ ID NO: 5 do not adequately support the scope of the recited genus, which encompasses a substantial variety of homologues or variants of the polypeptides of SEQ ID NO: 3. A description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant disclosure fails to provide sufficient description information, such as definitive structural or

functional features of the recited genus of GPCR variants and homologues. There is no description of the conserved regions that are critical to the structure and function of the genus recited. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function.

The prior art (U.S. 6,555,339 B1) teaches a GPR22, which is 99.5% identical to the amino acid sequence of SEQ ID NO: 3 and preparation of a non-endogenous and constitutively activated form of the GPR22 by site-directed mutagenesis (F312K). However, the prior art does not teach the ligand of the GPR22 and the physiological role of the GPR22 and does not provide compensatory structural or correlative teachings to enable one skilled in the art to identify the encompassed GPCR variants and homologues as being identical to those instantly claimed.

Moreover, the specification discloses the amino acid sequence of a first allele of human GPR22, SEQ ID NO: 2, and a second allele of human GPR22, SEQ ID NO: 3. However, there is no description of other mutational sites that exist in nature, and there is no description of how the structure of the polypeptides of SEQ ID NOS: 2 and 3 relates to the structure of different variants. The general knowledge in the art concerning variants does not provide any indication of how the structure of one variant is representative of other unknown variants having concordant or discordant functions. The nature of variants is such that they are variant structures where the structure and function of one does not provide guidance to the structure and function of others.

Due to the breadth of the genus of the GPCR variants recited in the claims and lack of the definitive structural or functional features of the recited genus, one skilled in the art would not recognize from the disclosure that the applicant was in possession of the genus of the polypeptides, and thus the instantly claimed methods.

(iv). Claims 140-144 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identifying a modulator of GPCR of SEQ ID NO: 3, does not reasonably provide enablement for a method of identifying a modulator of a GPCR comprising an amino acid sequence having at least 90% identity to SEQ ID NO: 3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims encompass a method of identifying a modulator of a genus of GPCR polypeptides comprising an amino acid sequence having at least 90% identity to SEQ ID NO: 3. The claims do not recite any structural or functional limitations for the variants and homologues. The specification fails to disclose the ligand that binds and activates the RUP41 polypeptides set forth in SEQ ID NO: 3. Without a known ligand, one skilled in the art would not be able to practice the instantly claimed method using a polypeptide that is not constitutively active. Thus, the instant disclosure fails to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claim Rejections Under 35 U.S.C. §112, 2nd Paragraph

(i). The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

(ii). Claims 132-147 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 132 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: how to determine the ability of a compound to modulate the G protein-coupled receptor; and how to determine whether a compound has cardioprotective activity. Likewise, claims 140 and 142 do not indicate how to mine whether a compound modulates survival or cardiomyocyte cell or cardiac function in the mammal. Moreover, these claims are so ambiguous that they fail to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Furthermore, claim 132 is indefinite because it recites “the ability of the compound to modulate the G protein-coupled receptor”. It is unclear what is to be modulated, rendering the claim indefinite. Likewise, claims 139 and 142 recite “which modulates the G protein-coupled receptor in (b)”. It is unclear what is to be modulated, rendering the claims indefinite.

Claims 136-139 are indefinite because it is unclear whether the limitations recited in the clams further limit (b) or (c) of the method of claim 132. Likewise, claim 141 is indefinite because it is unclear whether the limitation recited in claim 141 further limits (i) or (ii) of the method of claim 140.

Claim 145 is indefinite because the claim recites “wherein the candidate compounds are screened as pharmaceutical agents for congestive heart failure”. It is unclear whether the pharmaceutical agents are for treating congestive heart failure, rendering the claim indefinite.

Claim 145 recites the limitation "The method of claim 132, wherein the candidate compounds are screened”. There is insufficient antecedent basis for this limitation in claim 132. Claim 146 recites the limitation of “wherein the screen …”. There is insufficient antecedent basis for this limitation in claim 132, from which claim 145 depends.

Claims 133-135, 143, 144, and 147 are rejected as dependent claims from claim 132, either directly or indirectly.

Claim Objections —Minor Informalities

Claim 144 is objected to because it recites non-elected disease species (other than elected congestive heart failure). Appropriate correction is required.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875.

The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

/Ruixiang Li/
Primary Examiner, Art Unit 1646

Ruixiang Li, Ph.D.
February 25, 2008